C1
B5

28. (New) The nucleic acid of claim 1 wherein said salvage receptor comprises amino acids from 1 through about 11 of SEQ ID NO: 3 and amino acids from 1 through about 8 of SEQ ID NO: 31.

## REMARKS

Claim 1 has been amended. Claims 21 - 28 have been added and do not introduce new matter. Support for amended claim 1is found on page 2, line 35, page 6, lines 27-31, page 13, lines 30-33, page 20, lines 27-35, page 21, lines 1-35, and in Example 1, pages 54-56. Support for new claim 21 is found on page 13, lines 26-33. Support for new claims 22-24 is found on page 6, lines 13-16. Support for new claims 25-28 is found on page 14, lines 10-18, page 68, lines 16-30, page 69, lines 1-10, page 75, lines 19-29, and page 82, lines 31-35 and page 83, lines 1-5, and in Figures 2A and 2B.

Claims 1 and 21-28 are now pending.

**Claim Rejection - 35 USC §112, First Paragraph**

Claim 1 stands rejected under 35 USC §112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the invention at the time the application was filed. More particularly, the Examiner states that the disclosure does not provide an adequate description of the nucleic acids encoding the salvage receptor binding epitope that is claimed by Applicant.

Applicant respectfully traverses the rejection.

Applicant points out that claim 1 has been amended to recite nucleic acids encoding a modified polypeptide with an improved *in vivo* half-life, wherein the modified polypeptide comprises an Ig constant domain or Ig-like constant domain in combination with a salvage receptor binding epitope that is derived from a single loop of a $CH_2$ domain. Applicant has additionally added new claims 25-28 which particularly define the nucleic acids encoding the claimed salvage receptor binding epitope to those nucleotides encoding amino acids from 1 through about 11 of SEQ ID NO:3 (claim 25); nucleotides encoding amino acids from 1 through about 11 of SEQ ID NO:3 in combination with amino acids from 1 through about 7 of SEQ ID NO: 11 (claim 26); nucleotides encoding amino acids from 1 through about 11 of SEQ ID NO:3 in combination with amino acids from 1 through about 8 of SEQ ID NO: 1 (claim 27); and nucleotides encoding amino acids from 1 through about 11 of SEQ ID NO:3 in combination with amino acids from 1 through about 8 of SEQ ID NO: 31 (claim 28).

Support for amended claim 1 is found on page 2, line 35, page 6, lines 27-31, page 13, lines 30-33, page 20, lines 27-35, page 21, lines 1-35, and in Example 1, pages 54-56. Support for new claims 25-28 is found on page 14, lines 10-18, page 68, lines 16-30, page 69, lines 1-10, page 75, lines 19-29, and page 82, lines 31-35 and page 83, lines 1-5, and in Figures 2A and 2B.

Applicant submits that amended claim 1 and new claims 25-28 satisfy the requirements of 35 USC §112, first paragraph, since Applicant has particularly prescribed and defined the nucleic acids encoding the salvage receptor binding epitope. Because Applicant has provided an adequate description of the recited epitopes in structural terms, Applicant respectfully requests

reconsideration and withdrawal of the Examiner's outstanding rejection of amended claim 1 under 35 USC §112, first paragraph.

**Claim Rejection - 35 USC §102(b) As Being Anticipated by Pastan, et al. and Batra, et al.**

Claim 1 is rejected under 35 USC §102(b) as being anticipated by *Pastan, et al.* and *Batra, et al.*

Applicant respectfully traverses the rejection.

Applicant notes that *Pastan* teaches the production of recombinant protein chimeric toxins comprised of immunoglobulin domains (*e.g.*, $CH_2$, $CH_3$, $CH_1$-$CH_2$, or $CH_2$-$CH_3$) coupled to $CD_4$ receptor binding domains and cytotoxic exotoxin domains. Applicant's claims, in contrast, recite nucleic acids encoding immunoglobulin or immunoglobulin-like constant domains which do not encompass either a $CD_4$ receptor binding domain or cytotoxic exotoxin domain. The immunoglobulin or immunoglobulin-like constant domains encoded by Applicant's nucleotides contain a $CH_1$ domain (new claim 21), an Fab, $F(ab')_2$, or receptor (new claim 22), or an anti-CD18 Fab or anti-CD18 $F(ab')_2$ (new claim 23) wherein the immunoglobulin or immunoglobulin-like constant domain is specifically coupled to a salvage receptor binding epitope that is derived from a single loop of a $CH_2$ domain, wherein the salvage epitope increases the *in vivo* half-life of the modified polypeptide. The nucleic acids recited in Applicant's claims, as distinguished from the *Pastan* toxins, do not encode a chimeric toxin, and do not encode a polypeptide which contains either a $CD_4$ receptor binding or cytotoxic exotoxin domain.

Therefore, since *Pastan* does not describe each element of the claim, it cannot anticipate the claim.

Moreover, Applicant's claims are not anticipated by the *Batra* reference, which discloses the same chimeric toxins as *Pastan*.

For these reasons, Applicant respectfully requests that Examiner's rejection of amended claim 1 under 35 USC §102(b) be withdrawn and further maintains that new Claims 21-28 are not anticipated by the cited prior art.

**Claim Rejection - Nonstatutory Double Patenting**

Applicant requests that the double patenting rejection be held in abeyance until such time as patentable subject matter is found.

The Commissioner is authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our Order No. A-63470-7/RFT/NBC).

Please enter the following amended claim 1 along with the new claim set, and give favorable consideration to the remarks herein.

Respectfully submitted,

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ALBRITTON & HERBERT

Dated: March 4, 2002

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## VERSIONS WITH MARKINGS TO SHOW CHANGES MADE

**In the Specification:**

The paragraph beginning at page 1, line 1, has been amended as follows:

– This application is a continuation of Application No.:08/422,112, filed April 14, 1995, now Patent No. 6,121,022.–

The paragraph beginning at page 4, line 13, has been amended as follows:

– Figures 2A and 2B depict an alignment of the relevant portions of the consensus amino acid sequences of the human IgG1 CH1 domain (SEQ ID NO:4), the human IgG2 CH1 domain (SEQ ID NO: 5), the human IgG3 CH1 domain (SEQ ID NO: 6), the human IgG4 CH1 domain (SEQ ID NO: 7), the human kappa CL domain (SEQ ID NO: 8), and the human lamda CL domain (SEQ ID NO:9), in alignment with the Fab v1b variant derived from anti-CD18 antibody (SEQ ID NO:10), which is described in Example 1. In these figures, amino acid residues and/or positions of interest and of most importance to the invention within the sequence of Fab v1b (*i.e.*, SEQ ID NOS:3 and 1) are designated by underlining and asterisks, respectively.–

The paragraph beginning at page 6, line 27, has been amended as follows:

– As used herein, the term "salvage receptor binding epitope" refers to an epitope of the Fc region of an IgG molecule (e.g., IgG1, IgG2, IgG3, and IgG4) that is responsible for increasing the *in vivo* serum half-life of the IgG molecule. As an example, Figures 2A and 2B show representative epitopes in underlining and the important residues in asterisks. The IgG1, IgG2, and IgG4 isotypes are preferred for determining the salvage receptor binding eptiope.–

IN THE CLAIMS:

1. (Amended) A [N]nucleic acid encoding a modified polypeptide [variant of a polypeptide of interest which polypeptide of interest is cleared from the kidney and does not contain a Fc region of an IgG, which variant comprises a salvage receptor binding epitope of an Fc region of an IgG, and which variant has a longer] with an improved *in vivo* half-life [than the polypeptide of interest], said modified polypeptide comprising an Ig constant domain or Ig-like constant domain and a salvage receptor binding epitope within said Ig constant domain or Ig-like constant domain, wherein said epitope is absent from the unmodified polypeptide, wherein said salvage receptor epitope is taken from a loop of the $CH_2$ domain of an Fc region of an Ig molecule and wherein said polypeptide in modified form does not comprise an intact $CH_2$ domain or an intact Fc region.

21. (New) The nucleic acid of claim 1wherein the Ig domain or Ig-like domain comprises a CH1 domain.

22. (New) The nucleic acid of claim 1wherein the unmodified polypeptide is an Fab, an $(Fab')_2$, or a receptor.

23. (New) The nucleic acid of claim 22 wherein the unmodified polypeptide is an anti-CD18 Fab or an anti-CD18 $(Fab')_2$.

24. (New) The nucleic acid of claim 23 wherein the modified polypeptide is human or humanized.

25. (New) The nucleic acid of claim 1 wherein said salvage receptor epitope comprises amino acids from 1 through about 11 of SEQ ID NO: 3.

26. (New) The nucleic acid of claim 1 wherein said salvage receptor comprises amino acids from 1 through about 11 of SEQ ID NO: 3 and amino acids from1 through about 7 of SEQ ID NO: 11.

27. (New) The nucleic acid of claim 1 wherein said salvage receptor comprises amino acids from1 through about 11 of SEQ ID NO: 3 and amino acids from1 through about 8 of SEQ ID NO: 1.

28. (New) The nucleic acid of claim 1 wherein said salvage receptor comprises amino acids from1 through about 11 of SEQ ID NO: 3 and amino acids from1 through about 8 of SEQ ID NO: 31.